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EXAMINER	
BALLARD, KIMBERLY A	

ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/777,792	SCHENK ET AL.	
	Examiner	Art Unit	
	Kimberly A. Ballard	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 February 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-143* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-143* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/6/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Claim 131 has been amended as requested in the response filed February 6, 2007. Following the amendment, claims **119-143** are pending and under examination in the current office action.

Information Disclosure Statement

A signed and initialed copy of the IDS paper submitted February 6, 2007 is enclosed in this action.

Withdrawn Claim Rejections

The rejection of claims 131-143 under 35 U.S.C. 112, second paragraph, as set forth in the previous office action mailed August 7, 2006, is withdrawn in view of Applicants' amendment to claim 131.

Maintained Claim Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 119, 121-124, 126-131, 134-137, and 139-143 under 35 U.S.C. 103(a) as being unpatentable over WO 01/42306 A2 by Chain (as listed on Applicant's IDS), published 14 June 2001 (priority date: 8 December 1999), as evidenced by Alberts et al. (Molecular Biology of the Cell, 2nd Edn. Garland Publishing, New York, 1989, pp. 266-267), and in view of Frenkel et al. (*J Neuroimmunology*, March 1999; **95**: 136-142), US Patent No. 5,601,827 to Collier et al., issued 11 February 1997, and Van den Dobbelsteen et al. (*Scand J. Immunol*, 1995; **41**: 273-280) is maintained for reasons of record.

The claims are directed to a pharmaceutical composition comprising Aβ1-7 linked to CRM197 to form a conjugate, or a composition comprising an adjuvant and said conjugate (claims 119 and 131). Noted claim limitations include: the composition comprises at least 10, 20, 50, or 100 μg of Aβ1-7 (claims 121-124 and 134-137); wherein Aβ1-7 is linked to CRM197 at the amino or carboxyl terminus (claims 126, 127, 129, 130, 139, 140, 142, and 143); and wherein the conjugate is expressed as a fusion protein (claims 128 and 141).

In the response filed February 6, 2007, Applicants argue that one would not have been motivated to replace Chain's short peptide of up to five residues of Aβ with Aβ1-7 because Chain warns of the undesired outcome that using a longer peptide may generate antibodies that bind APP as well as Aβ causing undesired side effects, and thus Applicants assert that Chain teaches away from the claimed invention. Moreover, Applicants argue, Frenkel confirms Chain's concerns by reporting the presence of an epitope between residues of 3-6 of Aβ, wherein an immune response against this epitope, Applicants submit, would not be end-specific and would also be an immune response against APP. Applicants thus argue that using a longer peptide than is taught by Chain would defeat Chain's goal of producing only antibodies specific to the N-terminus of Aβ. Therefore, Applicants submit that there would be no motivation to replace Chain's short peptide of up to five residues of Aβ with Aβ1-7 because Chain warns of the undesired outcome that using a longer peptide may generate antibodies that bind APP as well as Aβ causing undesired side effects. Additionally, Applicants argue that Frenkel does not attach any particular significance to using an Aβ1-7

fragment to generate antibodies with anti-aggregating properties. Finally, Applicants assert that in view of the motivation for combining the references – i.e., for the treatment of Alzheimer's disease – the references do not provide a reasonable expectation of success of treating Alzheimer's disease using the claimed compositions.

Applicant's arguments have been fully considered but they are not persuasive. In response to applicant's argument that there is no motivation to combine the references to arrive at the claimed invention, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the knowledge generally available to one of ordinary skill in the art, as exemplified by (but not limited to) Chain and by Frenkel, would have provided the necessary motivation for combination of the references. At the time of filing, one of ordinary skill in the art would have been aware of studies demonstrating that immunization of transgenic PDAPP mice (which overexpress APP and develop brain pathology similar to what is observed with Alzheimer's disease) with full-length Aβ resulted in a reduction in amyloid plaque burden in the brains of the animals, which Applicant notes at p. 10 of the response was described by Schenk et al. (1999) (see also p. 6 of the Chain reference). Thus, one of ordinary skill in the art would have recognized that Aβ immunization is beneficial for reducing amyloid burden, and would therefore reasonably predict that

such immunization would be beneficial for the treatment of diseases related to abnormal amyloid deposition, such as Alzheimer's disease.

Chain is presented to broadly teach that chimeric peptides comprising end-specific Aβ peptides conjugated to a strong T helper cell epitope are useful as immunizing agents for the generation of anti-Aβ antibodies, because they can elicit a more specific and robust immunogenic response than would be achieved with Aβ peptide alone. The skilled artisan would also be aware of the fact that small peptide fragments of endogenous proteins are not particularly antigenic on their own (also noted at p. 7 of Chain), and thus coupling the peptide to a T-cell epitope, or administration with an adjuvant or both as taught by Chain, would be necessary in order to induce a sufficient immune response against the antigen. Frenkel teaches that monoclonal antibodies produced against the N-terminus of Aβ effectively inhibit the aggregation of Aβ protein, and thus demonstrates that the N-terminus of Aβ is crucial to the aggregating property of amyloid-beta protein. The monoclonal antibodies studied by Frenkel include 6C6 and 10D5, which were raised against Aβ 1-28, and 2H3, which was raised against Aβ 1-12. Thus, all of these antibodies were made by immunization with a fragment comprising Aβ 1-7. Both the 6C6 and 10D5 antibodies were particularly efficacious in interfering with the formation of b-amyloid fibrils. The fact that the mAb 2H3 (which recognizes an epitope within Aβ 1-7) failed to significantly interfere with fibril formation is beside the point, because the current invention is directed to a peptide construct, not a specific monoclonal antibody. Moreover, Chain notes that the peptide fragment Aβ 1-7 was capable of significantly inhibiting the binding not only of mAb 2H3,

but also of mAbs 6C6 and 10D5 (see Table 3 on p. 140), meaning that such a peptide would be useful for the production of a pharmaceutical composition such as instantly claimed..

The essential points that the skilled artisan would thus garner from Frenkel teachings are 1) that the N-terminus of Aβ is involved in Aβ fibril formation and aggregation, and 2) that it is possible to inhibit this aggregation with the use of specific antibodies that recognize an epitope comprising EFRH, or residues 3-6 of Aβ. Importantly, Frenkel notes that the amino acid residues 1-9 contribute mainly to the solubility of Aβ (see p. 140, 2nd column). And thus contrary to Applicants' assertions that using a longer peptide or using a peptide comprising the epitope of Aβ 3-6 would go against the teachings of Chain, one of skill in the art would, having taken all of the above teachings together as a whole, reasonably conclude that an N-terminal peptide comprising at least residues 3-6 of Aβ, such as the aforementioned Aβ 1-9, would be valuable as an immunizing agent for the treatment of conditions related to Aβ, such as Alzheimer's disease. It is noted that such a peptide would comprise Aβ 1-7, and would thus meet the limitations of the claimed composition. There is nothing in the Chain reference to contradict that using a peptide comprising at least residues 3-6 of Aβ would lead to the production of undesirable antibodies reactive against the precursor APP molecule. Moreover, immunization with a peptide comprising, for example, residues 1-9 of Aβ would induce a polyclonal antibody response wherein most of the antibodies would reasonably be expected to prove inhibitory to Aβ fibril formation and/or Aβ

aggregation, and thus would be therapeutically beneficial. Furthermore, MPEP § 2123 states that:

> A reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill the art, including nonpreferred embodiments. *Merck & Co. v. Biocraft Laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), *cert. denied*, 493 U.S. 975 (1989). See also *Upsher-Smith Labs. v. Pamlab, LLC*, 412 F.3d 1319, 1323, 75 USPQ2d 1213, 1215 (Fed. Cir. 2005)(reference disclosing optional inclusion of a particular component teaches compositions that both do and do not contain that component).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was filed to combine the teachings of Chain regarding chimeric peptides comprising end-specific Aβ peptides linked to a T-helper cell epitope, such as diphtheria toxin, with the teachings of Frenkel indicating that the N-terminus of Aβ comprises an epitope particularly important for inhibiting the fibrillogenic and neurotoxic properties of the Aβ peptide, along with the teachings of Collier and Van den Dobbelsteen, who direct the skilled artisan to the use of CRM-197, to arrive at the claimed pharmaceutical composition comprising an Aβ1-7/CRM197 conjugate. And with respect Applicants' assertions that the references do not provide a reasonable expectation of success of treating Alzheimer's disease, Applicant is reminded that the claimed composition is directed to a product and not a method of treatment. Therefore, the artisan would have a perfectly reasonable expectation that immunization with the chimeric peptide comprising Aβ peptide and CRM197 would be effective to induce a

robust anti-Aβ antibody response, and the N-terminal-specific antibodies elicited by this immune response would reasonably be expected to be capable of interfering with the formation of Aβ fibrils, as evidenced by the teachings of Frenkel. Thus, the claimed invention would be obvious in view of the relevant art at the time of filing.

The rejection of claims 120 and 132 under 35 U.S.C. 103(a) as being unpatentable over WO 01/42306 A2 by Chain, Alberts et al., and in view of Frenkel et al., Collier et al., and Van den Dobbelsteen et al., as applied to claims 119, 121-124, 126-131, 134-137, and 139-143 above, and further in view of US Patent Nos. 5,837,268 to Potter et al. and 5,733,548 to Restifo et al. is maintained for reasons of record.

The claims are directed to a pharmaceutical composition comprising Aβ1-7 linked to CRM197 to form a conjugate, or a composition comprising an adjuvant and said conjugate, wherein the conjugate comprises a plurality of additional copies of Aβ1-7.

In the response filed February 9, 2007, Applicants submit that claims 120 and 132 would have been non-obvious for at least the same reasons as claim 119 as above.

Applicant's arguments have been fully considered but they are not persuasive. The response to such arguments has been discussed above. Moreover, as noted in the previous office action, the teachings of Potter et al. and Restifo et al. are cumulative. Potter et al. notes that the art generally recognizes that the immunogenicity of viral antigens, small proteins or endogenous substances may be significantly increased by producing immunogenic forms of those molecules comprising multiple copies of selected epitopes (paragraph spanning column 1 – column 2, line 3). Restifo et al.

teach immunogenic chimeric proteins used *in vivo* to elicit specific T cell responses (see column 2, lines 53-57). Restifo discloses that multiple copies of a peptide, which may or may not be immunogenic by itself, may be contained within the immunogenic chimeric protein (see column 4, lines 32-36, and column 5, lines 15-22).

Thus, it would have been obvious to one of skill in the art at the time the invention was made to modify the chimeric peptide comprising Aβ1-7 linked to CRM-197, as discussed above, by inserting multiple copies of an Aβ peptide comprising Aβ1-7 within the chimeric peptide conjugate. The artisan would be motivated to make such a modification because both Potter and Restifo teach that the immunogenicity of a small endogenous protein can be enhanced by including multiple copies of such a peptide within the immunogenic chimeric protein. The peptide Aβ1-7 (or Aβ1-9 as above) is a small, endogenous protein and would not be predicted to be particularly immunogenic when administered by itself. The skilled artisan would therefore reasonably expect that including multiple copies of a peptide comprising Aβ1-7 within the chimeric Aβ/CRM-197 conjugate would enhance the immunogenic response when the chimeric peptide is administered as a pharmaceutical composition. Thus, the combined references render the claimed invention obvious to the artisan at the time the invention was made.

The rejection of claims 125 and 138 under 35 U.S.C. 103(a) as being unpatentable over WO 01/42306 A2 by Chain, as evidenced by Alberts et al., and in view of Frenkel et al., Collier et al., and Van den Dobbelsteen et al., as applied to claims

119, 121-124, 126-131, 134-137, and 139-143 above, and further in view of Peeters et al. (*J Immunol Methods*, 1989; **120**(1): 133-143) is maintained for reasons of record.

The claims are directed to a pharmaceutical composition comprising Aβ1-7 linked to CRM197 to form a conjugate, or a composition comprising an adjuvant and said conjugate, wherein Aβ1-7 is linked to CRM197 by chemical crosslinking.

In the response filed February 9, 2007, Applicants submit that claims 125 and 138 would have been nonobvious for at least the same reasons as claim 119 as above.

Applicant's arguments have been fully considered but they are not persuasive. The response to such arguments has been discussed above. Moreover, as noted in the previous office action, Peeters et al. compare the effects of four different cross-linking reagents on the immunogenicity of peptide-carrier conjugates used to raise anti-peptide antibodies. The four reagents studied included three of the "maleimide" type: succinimidyl 6-(*N*-maleimido)-*n*-hexanoate (MHS), succinimidyl 4-(*N*-maleimidomethyl)-cyclohexane-1-carboxylate (SMCC), and succinimidyl m-maleimidobenoate (MBS). Also studied was a coupling reagent containing an activated disulphide: succinimidyl 3-(2-pyridyldithio)propionate (SPDP) (see Abstract, p. 133). Peeters et al. note that in order to induce immunogenicity, peptides which do not generally elicit antibody production are coupled to macromolecular carriers (see paragraph spanning p. 133-135). Conjugation of peptides to other proteins by traditional methods can result in a great number of different products (i.e., "chaos" coupling; p. 135, 1st column). In order to obtain the best-defined product, Peeters notes, heterobifunctional cross-linkers should be used in such a way that the peptide will be coupled specifically and in a

predictable fashion to the carrier (see p. 135, 1st column); hence the use of reagents bearing a maleimide moiety (e.g., MHS, SMCC, and MBS) or activated disulphides (e.g., SPDP), each which couple peptide-carrier conjugates in a predictable manner (p. 135, 2nd and 3rd paragraphs). Peeters reports that compared to anti-peptide antibody titres to the unconjugated peptide, antibody titres were higher when the peptide was coupled to a carrier (in this case, tetanus toxoid) irrespective of the coupling method used (p. 142, 1st column). Finally, Peeters teaches that certain coupling reagents, such as MHS and SPDP, are preferred over SMCC and MBS in terms of their lower potential for immunogenicity, greater flexibility, and greater stability in aqueous solutions (p. 142, 2nd column).

Accordingly, it would have been obvious to one of skill in the art at the time the invention was made to conjugate the chimeric peptide comprising Aβ1-7 linked to CRM-197 (as discussed above) via chemical crosslinking reagents which conjugate in a predictable fashion, such as, preferably, MHS and SPDP, and also SMCC and MBS, as taught by Peeters et al. The artisan would be motivated to use such reagents because Peeters teaches that conjugation of peptides to carrier proteins using other reagents which conjugate the proteins in a non-predictable manner result in chaotic coupling and products that vary greatly in size and structure. Such variability is undesirable as the "chaotic" immunogenic peptides could elicit the production of antibodies that do not bind to the desired epitope comprising Aβ1-7 (and more specifically Aβ 3-6) but instead react with the linker region. The skilled artisan would be further motivated to chemically crosslink a peptide comprising Aβ1-7 to CRM-197 using a reagent such as MHS or

SPDP because Peeters teaches that such reagents are less immunogenic, more stable, and provide greater flexibility than the other reagents studied whilst still retaining high level of antibody production to the peptide-carrier conjugate. The skilled artisan would therefore reasonably expect that conjugating an Aβ peptide to CRM-197 via chemical crosslinking would result in uniform chimeric peptides which retain high immunogenicity to the desired epitope and not the linker reagent. Thus, the combined references render the claimed invention obvious to the artisan at the time the invention was made.

The rejection of claim 133 under 35 U.S.C. 103(a) as being unpatentable over WO 01/42306 A2 by Chain, as evidenced by Alberts et al., and in view of Frenkel et al., US Patent No. 5,601,827 to Collier et al., and Van den Dobbelsteen et al., as applied to claims 119, 121-124, 126-131, 134-137, and 139-143 above, and further in view of WO 99/10008 by Kensil et al., published 4 March 1999, filed 29 August 1997, is maintained for reasons of record.

The claims are directed to a pharmaceutical composition comprising Aβ1-7 linked to CRM197 to form a conjugate, said composition also comprising an adjuvant, wherein the adjuvant comprises QS-21.

In the response filed February 9, 2007, Applicants submit that claims 125 and 138 would have been nonobvious for at least the same reasons as claim 119 as above.

Applicant's arguments have been fully considered but they are not persuasive. The response to such arguments has been discussed above. Additionally, Kensil et al. teach the use of the adjuvant saponin QS-21 to be employed with vaccines comprising

proteins or peptides (see Abstract). Kensil teaches that QS-21 is useful as an immune adjuvant for enhancing immune responses in individuals at a much lower concentration than previously available heterogeneous saponin preparations without the toxic effects associated with crude saponin preparations (p. 1, lines 22-26). Kensil discloses compositions comprising a saponin adjuvant, such as QS-21, an antigen, and an excipient (paragraph spanning pp. 10-11). Kensil teaches that saponins such as QS-21 may be utilized to enhance the immune response to any antigen, such as proteins, peptides, nucleic acids, etc., which may be purified from a natural source, synthesized by means of solid phase synthesis, or obtained by means of recombinant genetics (paragraph spanning pp. 11-12). Kensil also teaches compositions comprising QS-21 that reduce the lytic effect of QS-21 and/or stabilize (increase the half-life of) QS-21 (see Examples 1 and 2, pp. 14-21).

It would have been obvious to one of skill in the art at the time the invention was made to use the adjuvant QS-21, as taught by Kensil et al., in a composition comprising a chimeric peptide comprising Aβ1-7 linked to CRM-197 peptide conjugate (as discussed above) to enhance the immune response to the conjugated peptide. The skilled artisan would be motivated to use QS-21 as an adjuvant because Kensil teaches that QS-21 is useful in vaccine preparations for enhancing immune responses at lower doses and with less toxic side-effects than other crude saponin adjuvant preparations. The skilled artisan would be further motivated to use QS-21 because Kensil teaches QS-21 compositions with significantly improved properties relevant to the lytic effect, tolerance to QS-21 associated pain, and product stability of QS-21, while still

maintaining full adjuvant activity. The skilled artisan would therefore reasonably expect that use of the adjuvant QS-21 in a composition further comprising an Aβ linked to CRM-197 would enhance the immunogenicity of the chimeric peptide conjugate. Thus, the combined references render the claimed invention obvious to the artisan at the time the invention was made.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly A. Ballard whose telephone number is 571-272-4479. The examiner can normally be reached on Monday-Friday 9AM - 5:30PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

Kimberly Ballard, Ph.D.
April 25, 2007

ELIZABETH C. KEMMERER. PH.D.
PRIMARY EXAMINER